

REMARKS

Upon entry of the present amendment, claims 2, 3, 12, 32 and 37 have been amended, and claims 2-8, 12, 14, 24 and 32-50 are pending. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made".

Claim Rejections - 35 USC §102

a. Claims 2, 3, 12, 32-36, 38, 39 and 49 have been amended to delete the double inclusion of the definition of R¹³.

b. Claim 37 has been amended to delete "reactive groups".

c. Claims 2, 3, 12 and 32 have been amended to more clearly describe the proviso for G.

Claim Rejections - 35 USC 102


Claims have been amended to change the proviso in G. Hence, the provisos for G now distinguish all of the cited references.

Conclusions

In view of the above amendments and remarks, applicants respectfully request that the pending claims be passed to issue. The Commissioner is hereby authorized to charge any additional fees which may be required in this application to Deposit Account No. 06-1135.

Respectfully submitted,

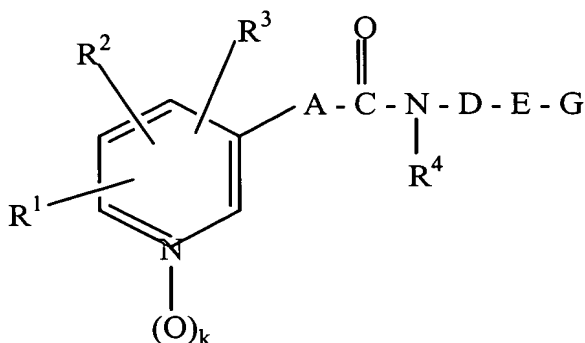
FITCH, EVEN, TABIN & FLANNERY

By 
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Version with Markings to Show Changes Made

2. (three times amended) Pyridylalkane, pyridylalkene and pyridylalkine carboxamides of formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_2 - C_6 -alkinyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, C_3 - C_6 -alkinyloxy, benzyloxy, C_1 - C_7 -alkanoyloxy, C_2 - C_7 -alkoxycarbonyloxy, C_1 - C_6 -alkylthio, C_3 - C_6 -alkenylthio, C_3 - C_6 -alkinylthio, C_3 - C_8 -cycloalkyloxy, C_3 - C_8 -cycloalkylthio, C_2 - C_7 -alkoxycarbonyl, aminocarbonyl, C_2 - C_7 -alkylaminocarbonyl, C_3 - C_{13} -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, C_1 - C_6 -alkoxy, benzyloxy and C_1 - C_7 -alkanoyloxy;

R^1 and R^2 , if adjacent, may form a bridge selected from $-(CH_2)_4-$ and $-(CH=CH)_2-$ or $CH_2O-CR^7R^8-O-$, wherein R^7 and R^8 are selected independently from each other from hydrogen and C_1 - C_6 -alkyl;

R^3 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and C_1 - C_6 -hydroxyalkyl;

R^4 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_6 -cycloalkyl, hydroxy, C_1 - C_6 -alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C_1 - C_6 -alkylene,

a substituted C_1 - C_6 -alkylene which is substituted one to three-fold by C_1 - C_3 -alkyl, hydroxy, C_1 - C_3 -alkoxy, fluorine, or phenyl,

C_2 - C_6 -alkylene, in which a methylene unit is isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R^9 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_1 - C_6 -acyl and C_1 - C_6 -alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

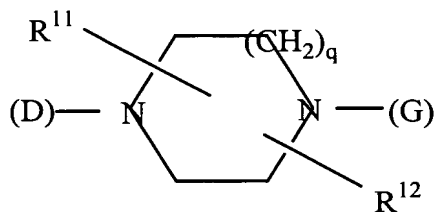
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R¹¹ is selected from the group consisting of hydrogen C₁-C₆-alkyl, hydroxy, hydroxymethyl, carboxy, or C₂-C₇-alkoxycarbonyl,

R¹² is selected from the group consisting of hydrogen, C₁-C₆-alkyl and an oxo group adjacent to a nitrogen atom,

and wherein R¹¹ and R¹² may together form a C₁-C₃-alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G¹ is - (CH₂)_r - (CR¹⁴R¹⁵)_s - R¹³

r is 0, 1, 2 or 3,

s is 0 or 1,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₈-cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage may occur either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R^{14} has the same meaning as R^{13} , but is selected independently thereof;

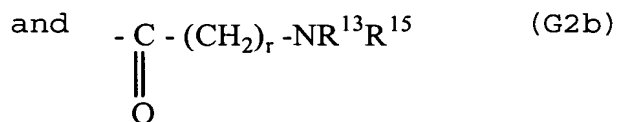
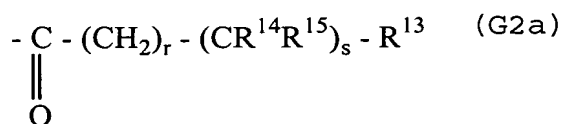
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

G^2 is selected from the group consisting of



wherein r , s and the substituents R^{13} to R^{15} can have the above meaning, or the group $-NR^{13}R^{15}$ is a nitrogen containing heterocycle,

wherein $-NR^{13}R^{15}$ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

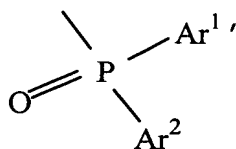
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$

wherein r and R^{13} have the above meanings,

G^4 is



wherein

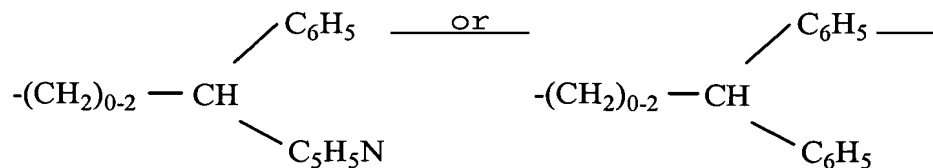
Ar¹ and Ar² are selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G⁵ is -COR¹⁶

R¹⁶ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, and benzyloxy,

wherein G is not -(CH₂)_r-(CR¹⁴R¹⁵)_s-R¹³ when
 R¹³ represents pyridyl or phenyl, which may be substituted by halogen, alkyl, alkoxy or trifluoromethyl,
 R¹⁴ represents hydrogen or phenyl, which may be substituted by halogen, alkyl, alkoxy or trifluoromethyl,
 R¹⁵ represents hydrogen,
 A represents alkylene, substituted ethenylene or butadienylene,
 D represents alkylene or alkenylene,
 E represents piperazine or homopiperazine, and
 s is 1;

wherein G is not phenyl, N-containing heteroaryl, -(CH₂)₀₋₂-CH₂-C₆H₅, -(CH₂)₀₋₂-CH₂-C₅H₅N,



wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy.

[or

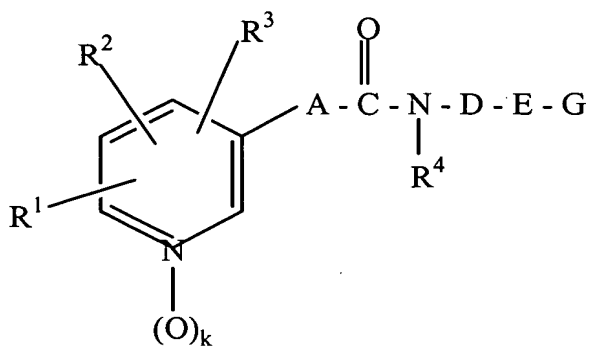
- (CH₂)_{ma}-CHR^{10a11a}, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy;]

when

- R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₈-cycloalkyloxy, a C₃-C₈-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;
- R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or -CH₂OCR^{8a}R^{9a}O-, wherein R^{8a} and R^{9a} are the same or different and are each a C₁-C₆-alkyl;
- R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;
- A is a C₁-C₆-alkylene or -(CR^{6a}=CR^{7a})ra-, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;
- R⁴ is hydrogen;
- D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and
- E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

3. (Twice amended) A compound according to formula (I)



(I)

wherein

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_1 - C_4 -alkylthio, C_1 - C_5 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_2 - C_5 -alkylaminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, and C_1 - C_4 -alkoxy;

R^3 is selected from the group consisting of hydrogen, halogen and C_1 - C_6 -alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and, the residue R⁹, is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₁-C₆-acyl and methane sulfonyl;

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once to twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

C₄-C₁₀-alkenylene,

a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

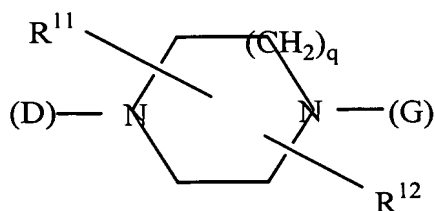
C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkinylene, wherein one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein

R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy, and C_2 - C_7 -alkoxycarbonyl and

R^{12} is selected from the group consisting of hydrogen, and an oxo group adjacent to a nitrogen atom,

and wherein R^{11} and R^{12} may together form a C_1 - C_3 -alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0, 1 or 2,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl; benzyl, phenyl;

monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O, wherein the linkage occurs either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R^{14} has the same meaning as R^{13} , but is selected independently thereof;

R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

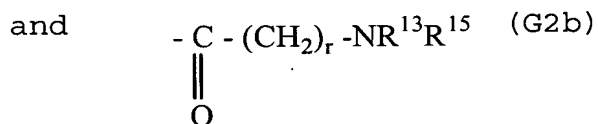
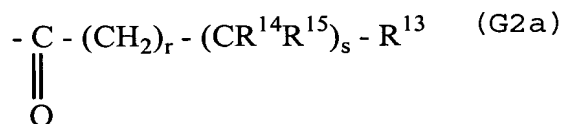
monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs

either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms can be selected from N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group;

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵ is a nitrogen containing heterocycle,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle selected from the group consisting of

[saturated or unsaturated monocyclic, four to eight-membered heterocycles,]

saturated or unsaturated monocyclic, four to eight-membered heterocycles which aside from the essential nitrogen

atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

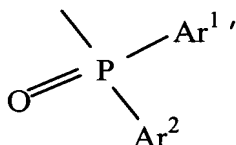
saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms that aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from the group consisting of N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$

wherein r and R^{13} have the above meaning,

G^4 is



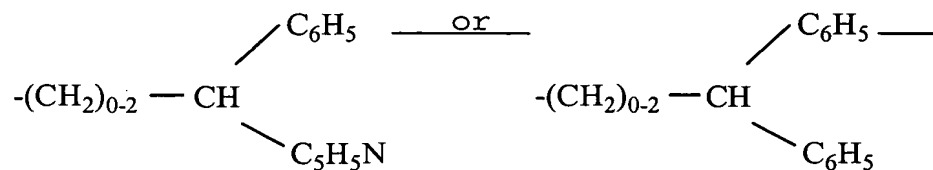
wherein

Ar^1 and Ar^2 are be selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G^5 is $-\text{COR}^{16}$

R^{16} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, and benzyloxy, wherein G is not phenyl, N-containing heteroaryl,

$-(\text{CH}_2)_{0-2}-\text{CH}_2-\text{C}_6\text{H}_5$, $-(\text{CH}_2)_{0-2}-\text{CH}_2-\text{C}_5\text{H}_5\text{N}$



wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy,

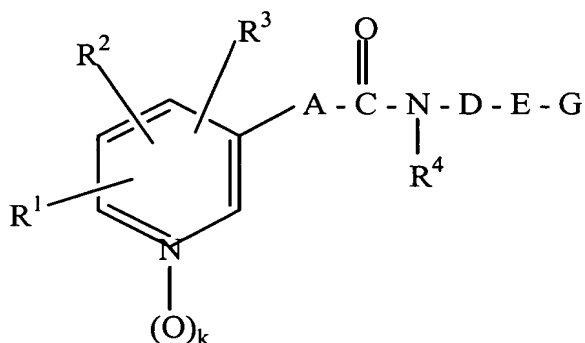
[-(CH₂)_{ma}-CHR^{10a}R^{11a}, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy;] when

- R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₈-cycloalkyloxy, a C₃-C₈-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;
- R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or -CH₂OCR^{8a}R^{9a}O-, wherein R^{8a} and R^{9a} are the same or different and are each a C₁-C₆-alkyl;
- R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;
- A is a C₁-C₆-alkylene or -(CR^{6a}=CR^{7a})ra-, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;
- R⁴ is hydrogen;

- D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and
- E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

12. (four times amended) A pharmaceutical composition comprising the compound of formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkinyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkinylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy,

phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, benzyloxy and $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$;

R^3 is selected from the group consisting of hydrogen, halogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl and $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$;

R^4 is selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$ and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of $\text{C}_1\text{-C}_6\text{-alkylene}$,

a substituted $\text{C}_1\text{-C}_6\text{-alkylene}$ which is substituted one to three-fold by $\text{C}_1\text{-C}_3\text{-alkyl}$, hydroxy, $\text{C}_1\text{-C}_3\text{-alkoxy}$, fluorine, or phenyl,

$\text{C}_2\text{-C}_6\text{-alkylene}$, in which a methylene unit is isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R^9 is selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, $\text{C}_1\text{-C}_6\text{-acyl}$ and $\text{C}_1\text{-C}_6\text{-alkanesulfonyl}$,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

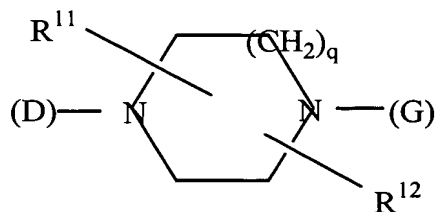
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkinylene,

a substituted C_4 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_6 -alkyl, hydroxy, or C_1 - C_6 -alkoxy; and

C_2 - C_{10} -alkylene, C_4 - C_{10} -alkenylene or C_4 - C_{10} -alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR^{10} , CO, SO, or SO_2 , wherein R^{10} has the same meaning as R^9 , but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₈-cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R^{14} has the same meaning as R^{13} , but is selected independently thereof;

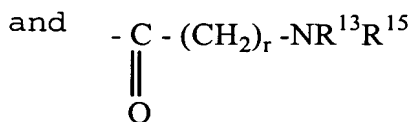
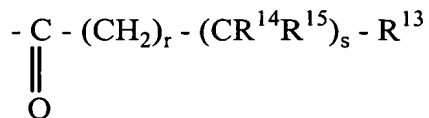
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

G^2 is selected from the group consisting of



wherein r, s and the substituents R^{13} to R^{15} can have the above meaning, or the group $-NR^{13}R^{15}$,

wherein $-NR^{13}R^{15}$ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

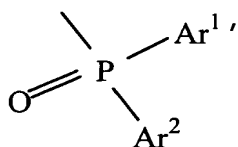
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-R^{13}$ (G^3)

wherein r and R^{13} have the above meanings,

G^4 is



wherein

Ar¹ and Ar² are selected independently from each other from phenyl, pyridyl or naphthyl,

G⁵ is -COR¹⁶ (G5)

R¹⁶ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, and benzyloxy,

wherein G is not -(CH₂)_r-(CR¹⁴R¹⁵)_s-R¹³ when
R¹³ represents pyridyl or phenyl, substituted by halogen, alkyl, alkoxy or trifluoromethyl,

R¹⁴ represents hydrogen or phenyl, substituted by halogen, alkyl, alkoxy or trifluoromethyl,

R¹⁵ represents hydrogen,

A represents alkylene, substituted ethenylene or butadienylene,

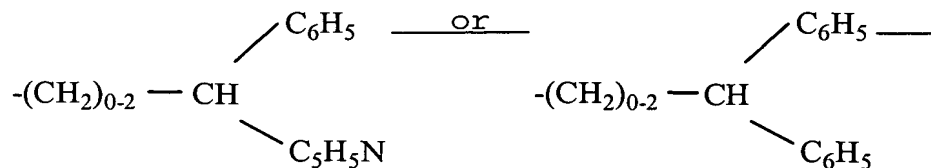
D represents alkylene or alkenylene,

E represents piperazine or homopiperazine, and

S is 1;

wherein G¹ is not phenyl, N-containing heteroaryl,

-(CH₂)₀₋₂-CH₂-C₆H₅, -(CH₂)₀₋₂-CH₂-C₅H₅N,



wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy,

[or $(-\text{CH}_2)_{\text{ma}}-\text{CHR}^{10\text{a}}\text{R}^{11\text{a}}$, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy;] when

R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₈-cycloalkyloxy, a C₃-C₈-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;

R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or $-\text{CH}_2\text{OCR}^{8\text{a}}\text{R}^{9\text{a}}\text{O}-$, wherein R^{8a} and R^{9a} are the same or different and are each a C₁-C₆-alkyl;

R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;

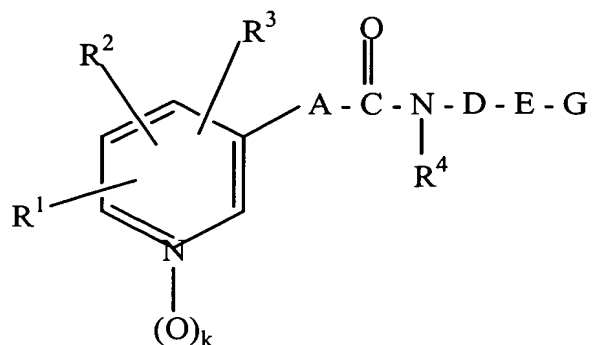
A is a C₁-C₆-alkylene or $-(\text{CR}^{6\text{a}}=\text{CR}^{7\text{a}})\text{ra}-$, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;

R⁴ is hydrogen;

D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and

E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

32. (Twice amended) A pharmaceutical composition comprising the compound of formula (I)



(I)

wherein

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_4 -alkoxy, benzyloxy, C_1 - C_4 -alkylthio, C_1 - C_5 -alkanoyloxy, C_1 - C_4 -alkylthio, C_2 - C_5 -alkoxycarbonyl, aminocarbonyl, C_2 - C_5 -alkylaminocarbonyl, C_3 - C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from hydrogen and C_1 - C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, and C_1 - C_4 -alkoxy;

R^3 is selected from the group consisting of hydrogen, halogen and C_1 - C_6 -alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and, the residue R⁹, is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₁-C₆-acyl and methane sulfonyl;

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once to twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

C₄-C₁₀-alkenylene,

a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

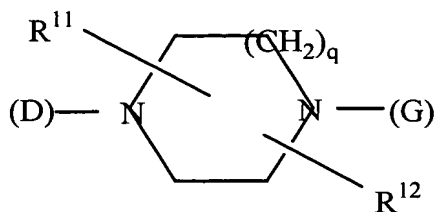
C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkinylene, wherein one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein

R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_3 -alkyl, hydroxy, hydroxymethyl, carboxy, and C_2 - C_7 -alkoxycarbonyl and

R^{12} is selected from the group consisting of hydrogen, and an oxo group adjacent to a nitrogen atom,

and wherein R^{11} and R^{12} may together form a C_1 - C_3 -alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0, 1 or 2,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl; benzyl, phenyl;

monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O, wherein the linkage occurs either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R¹⁴ has the same meaning as R¹³, but is selected independently thereof;

R¹⁵ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

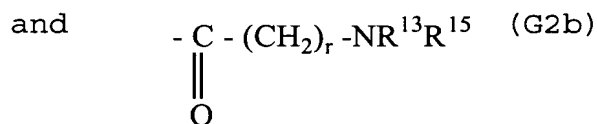
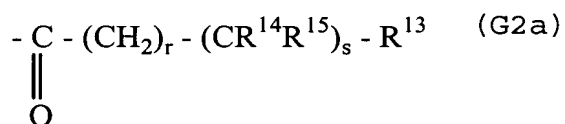
monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs

either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms can be selected from N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group;

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵ is a nitrogen containing heterocycle,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle selected from the group consisting of

[saturated or unsaturated monocyclic, four to eight-membered heterocycles,]

saturated or unsaturated monocyclic, four to eight-membered heterocycles which aside from the essential nitrogen

atom contain one or two further hetero-atoms selected from the group consisting of N, S and O,

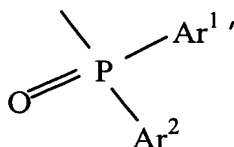
saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms that aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from the group consisting of N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$

wherein r and R^{13} have the above meaning,

G^4 is



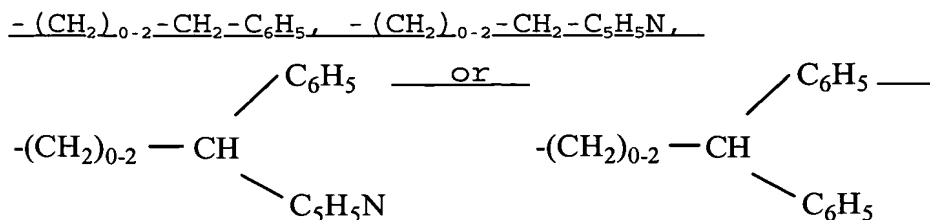
wherein

Ar^1 and Ar^2 are be selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G^5 is $-\text{COR}^{16}$

R^{16} is selected from the group consisting of trifluoromethyl, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$, and benzyloxy,

wherein G is not phenyl, N-containing heteroaryl,



wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy,

[or $(\text{-CH}_2)_{ma}\text{-CHR}^{10a}\text{R}^{11a}$, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy;] when

R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₈-cycloalkyloxy, a C₃-C₈-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;

R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or $\text{-CH}_2\text{OCR}^{8a}\text{R}^{9a}\text{O-}$, wherein R^{8a} and R^{9a} are the same or

different and are each a C₁-C₆-alkyl;

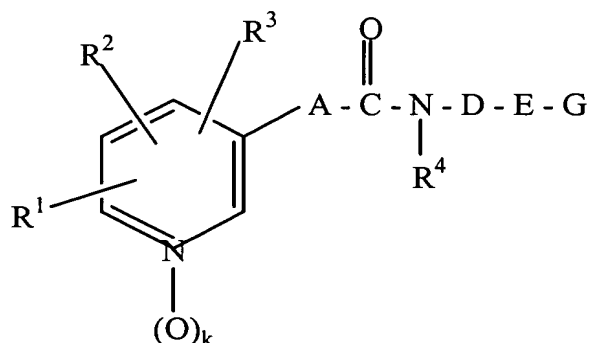
R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;

A is a C₁-C₆-alkylene or $\text{-(CR}^{6a}\text{=CR}^{7a}\text{)ra-}$, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;

R⁴ is hydrogen;

- D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and
- E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

33. (Once amended) A method of inhibiting tumor cell growth in a human or animal body comprising administering to the human or animal body in need thereof an amount of a pharmaceutical composition effective for inhibiting tumor cell growth, wherein the pharmaceutical composition includes a compound of general formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkinyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkinylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-

cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR⁵R⁶, wherein

R⁵ and R⁶ are selected independently of each other from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, benzyl and phenyl;

R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of

hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

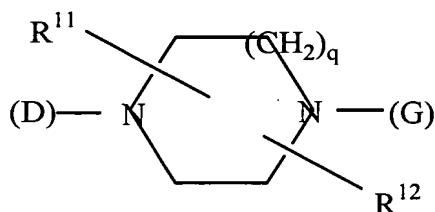
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R¹¹ is selected from the group consisting of hydrogen C₁-C₆-alkyl, hydroxy, hydroxymethyl, carboxy, or C₂-C₇-alkoxycarbonyl,

R¹² is selected from the group consisting of hydrogen, C₁-C₆-alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G¹ is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₈-cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and

the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

R^{14} has the same meaning as R^{13} , but is selected independently thereof;

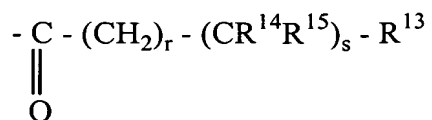
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

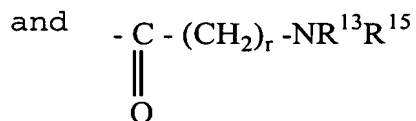
monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

G^2 is selected from the group consisting of





wherein r, s and the substituents R^{13} to R^{15} can have the above meaning, or the group $\text{-NR}^{13}\text{R}^{15}$,

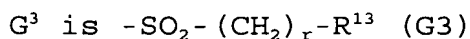
wherein $\text{-NR}^{13}\text{R}^{15}$ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

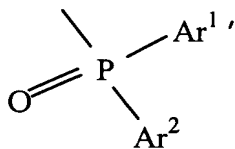
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from N, S and O;



wherein r and R^{13} have the above meanings,

G^4 is



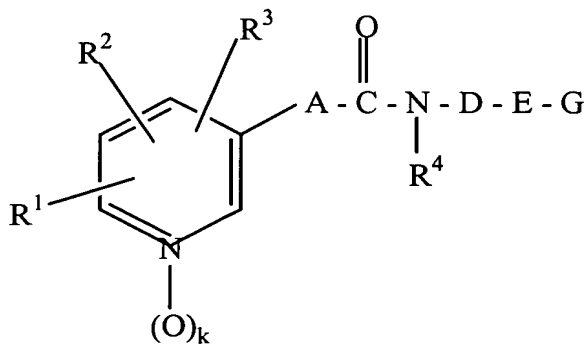
wherein

Ar¹ and Ar² are selected independently from each other from phenyl, pyridyl or naphthyl,

G⁵ is -COR¹⁶

R¹⁶ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, and benzyloxy.

34. (Once amended) A method of suppressing autoimmune diseases in a human or animal body comprising administering to the human or animal body in need thereof an amount of a pharmaceutical composition effective for suppressing autoimmune reactions, wherein the pharmaceutical composition includes a compound of general formula (I)



(I)

wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkinyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkinylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR⁵R⁶, wherein

R⁵ and R⁶ are selected independently of each other from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, benzyl and phenyl;

R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C_2 - C_{10} -alkylene which is substituted once or twice by C_1 - C_6 -alkyl, hydroxy, or C_1 - C_6 -alkoxy;

C_4 - C_{10} -alkenylene,

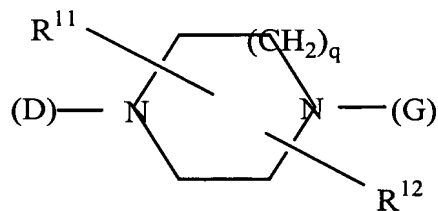
a substituted C_4 - C_{10} -alkenylene which is substituted once or twice by C_1 - C_6 -alkyl, hydroxy, or C_1 - C_6 -alkoxy;

C_4 - C_{10} -alkynylene,

a substituted C_4 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_6 -alkyl, hydroxy, or C_1 - C_6 -alkoxy; and

C_2 - C_{10} -alkylene, C_4 - C_{10} -alkenylene or C_4 - C_{10} -alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR^{10} , CO, SO, or SO_2 , wherein R^{10} has the same meaning as R^9 , but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms

and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

R¹⁴ has the same meaning as R¹³, but is selected independently thereof;

R¹⁵ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

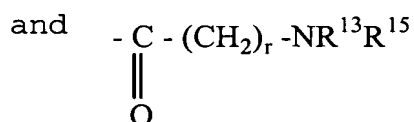
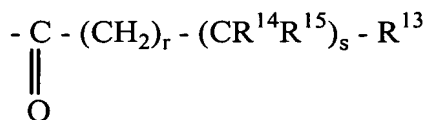
monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and

the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

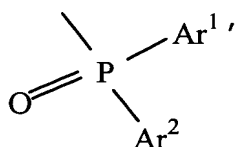
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain

one or two further hetro-atoms that are selected from N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$ ($G3$)

wherein r and R^{13} have the above meanings,

G^4 is



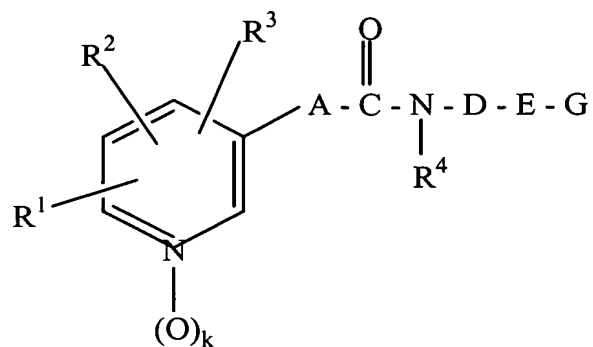
wherein

Ar^1 and Ar^2 are selected independently from each other from phenyl, pyridyl or naphthyl,

G^5 is $-\text{COR}^{16}$

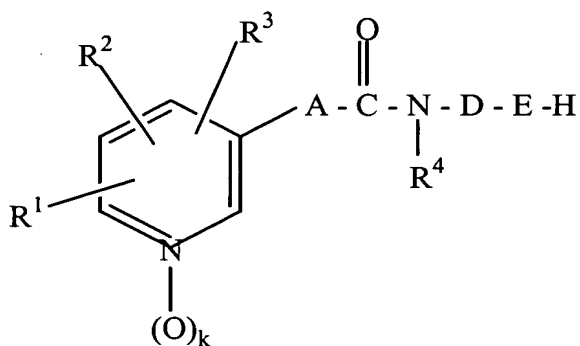
R^{16} is selected from the group consisting of trifluoromethyl, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$, and benzyloxy.

35. (Once amended) A method for production of compounds according to formula (I)



(I)

wherein compounds of a formula



are reacted with a compound of formula (IV)

L - G (IV)

wherein G is not hydrogen and is defined below, and L is a leaving group selected from the group consisting of alcohol, chlorine, bromine, iodine, sulfonic acid ester, methanesulfonyloxy, trifluoromethanesulfonyloxy, ethanesulfonyloxy, benzensulfonyloxy, p-toluenesulfonyloxy, p-

bromobenzenesulfonyloxy, m-nitrobenzenesulfonyloxy, and a terminal epoxide group,

wherein the reaction occurs in an inert solvent at a temperature between about 0°C and about 180°C., wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkinyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkinylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR⁵R⁶, wherein

R⁵ and R⁶ are selected independently of each other from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, benzyl and phenyl;

R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of
C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

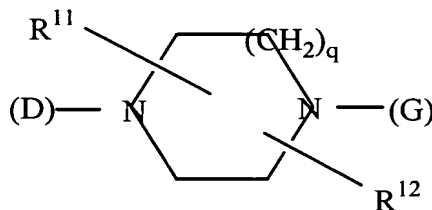
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles

which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

R¹⁴ has the same meaning as R¹³, but is selected independently thereof;

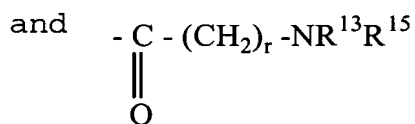
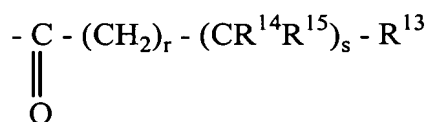
R¹⁵ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

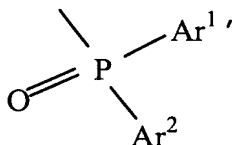
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetro-atoms that are selected from N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$ ($G3$)

wherein r and R^{13} have the above meanings,

G^4 is



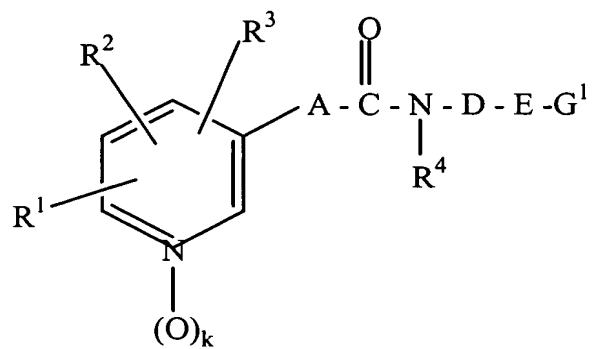
wherein

Ar^1 and Ar^2 are selected independently from each other from phenyl, pyridyl or naphthyl,

G^5 is $-\text{COR}^{16}$

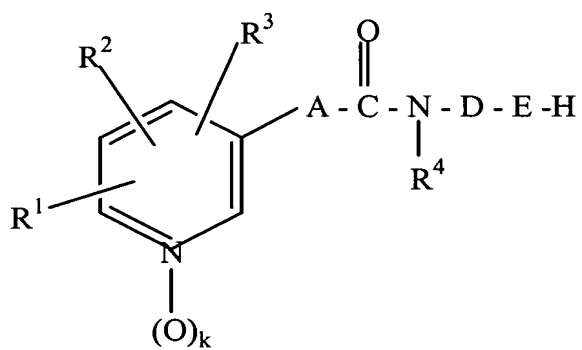
R^{16} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, and benzyloxy.

36. (Once amended) A method for production of compounds according to formula (I)



(I)

wherein compounds of a formula



are reacted with a compound of formula (IV)

L - G (IV)

wherein G is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl and heteroaralkyl,

wherein L is a leaving group selected from the group consisting of alcohol, chlorine, bromine, iodine, sulfonic acid ester, methanesulfonyloxy, trifluoromethanesulfonyloxy, ethanesulfonyloxy, benzensulfonyloxy, p-toluenesulfonyloxy, p-bromobenzenesulfonyloxy, m-nitrobenzenesulfonyloxy, and a terminal epoxide group,

wherein the reaction occurs in an inert solvent at a temperature between about 0°C and about 180°C., wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkynyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkynyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkynylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR⁵R⁶, wherein

R⁵ and R⁶ are selected independently of each other from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, benzyl and phenyl;

R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

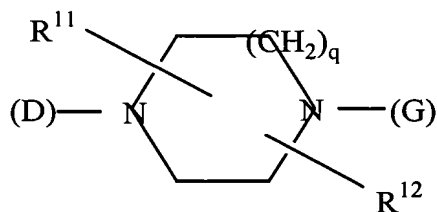
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

R¹⁴ has the same meaning as R¹³, but is selected independently thereof;

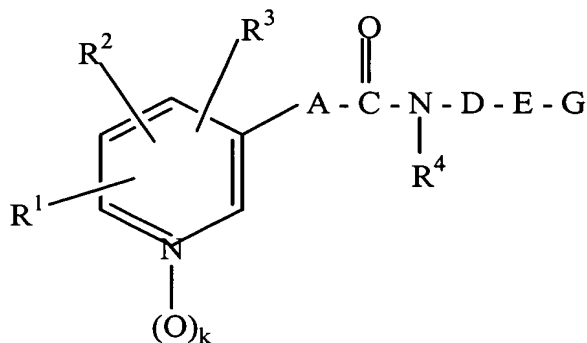
R¹⁵ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group.

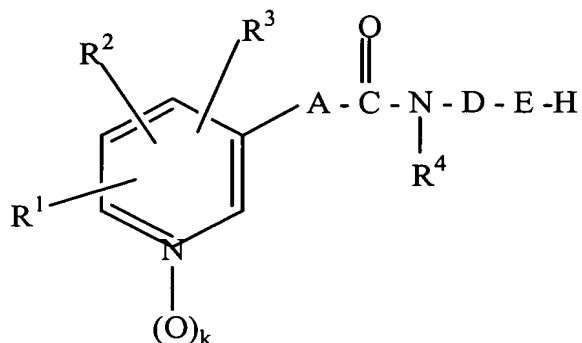
37. (Twice amended) A method for production of compounds according to formula (I)



(I)

wherein G is selected from the group consisting of an acyl residue, a carbamoyl residue, a sulfonyl residue and a phosphinoyl residue,

wherein compounds of a formula



are reacted with a compound of formula (V)



wherein G is selected from the group consisting of acyl residues, carbamoyl residues, sulfonyl residues, and phosphinoyl residues, [and their reactive derivatives,]

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_2 - C_6 -alkinyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, C_3 - C_6 -alkinyloxy, benzyloxy, C_1 - C_7 -alkanoyloxy, C_2 - C_7 -alkoxycarbonyloxy, C_1 - C_6 -alkylthio, C_3 - C_6 -alkenylthio, C_3 - C_6 -alkinylthio, C_3 - C_8 -cycloalkyloxy, C_3 - C_8 -cycloalkylthio, C_2 - C_7 -alkoxycarbonyl, aminocarbonyl, C_2 - C_7 -alkylaminocarbonyl, C_3 - C_{13} -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, benzyl and phenyl;

R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

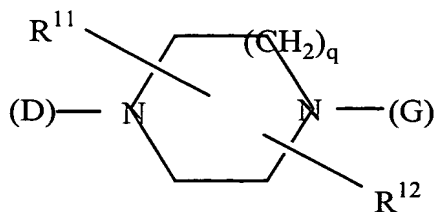
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C_2 - C_{10} -alkylene, C_4 - C_{10} -alkenylene or C_4 - C_{10} -alkinylene, in which one to three methylene units are isosterically replaced by O, S, NR^{10} , CO, SO, or SO_2 , wherein R^{10} has the same meaning as R^9 , but is selected independently thereof;

E is



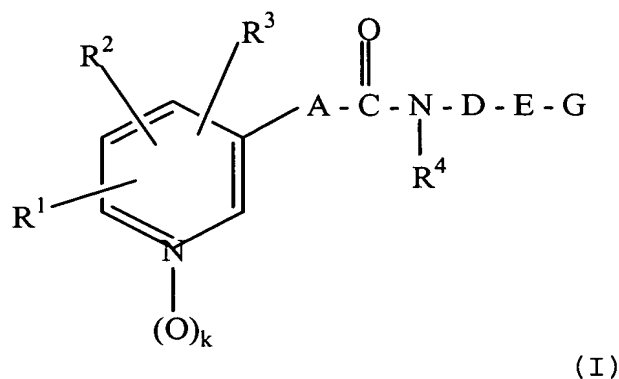
wherein

q is 1, 2, or 3;

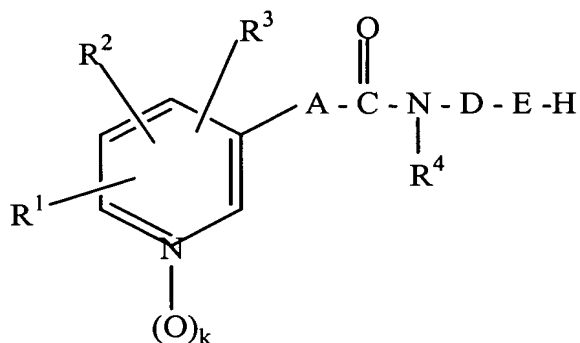
R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom.

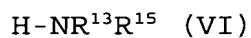
38. (Once amended) A method for production of compounds according to formula (I)



wherein compounds of a formula



are reacted with a carbonyl group transmitter to an intermediate product which is reacted with a primary or secondary amine having the formula (VI)



wherein:

R¹ is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₂-C₆-alkinyl, trifluoromethyl, C₃-C₈-cycloalkyl, C₁-C₆-hydroxyalkyl, hydroxy, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, C₃-C₆-alkinyloxy, benzyloxy, C₁-C₇-alkanoyloxy, C₂-C₇-alkoxycarbonyloxy, C₁-C₆-alkylthio, C₃-C₆-alkenylthio, C₃-C₆-alkinylthio, C₃-C₈-cycloalkyloxy, C₃-C₈-cycloalkylthio, C₂-C₇-alkoxycarbonyl, aminocarbonyl, C₂-C₇-alkylaminocarbonyl, C₃-C₁₃-dialkylaminocarbonyl, carboxy,

phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, benzyloxy and $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$;

R^3 is selected from the group consisting of hydrogen, halogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl and $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$;

R^4 is selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, $\text{C}_3\text{-C}_6\text{-cycloalkyl}$, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$ and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of $\text{C}_1\text{-C}_6\text{-alkylene}$,

a substituted $\text{C}_1\text{-C}_6\text{-alkylene}$ which is substituted one to three-fold by $\text{C}_1\text{-C}_3\text{-alkyl}$, hydroxy, $\text{C}_1\text{-C}_3\text{-alkoxy}$, fluorine, or phenyl,

$\text{C}_2\text{-C}_6\text{-alkylene}$, in which a methylene unit is isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R^9 is selected from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, $\text{C}_1\text{-C}_6\text{-acyl}$ and $\text{C}_1\text{-C}_6\text{-alkanesulfonyl}$,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

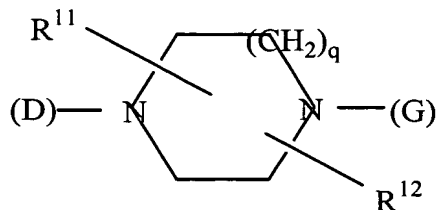
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkinylene,

a substituted C_4 - C_{10} -alkynylene which is substituted once or twice by C_1 - C_6 -alkyl, hydroxy, or C_1 - C_6 -alkoxy; and

C_2 - C_{10} -alkylene, C_4 - C_{10} -alkenylene or C_4 - C_{10} -alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR^{10} , CO, SO, or SO_2 , wherein R^{10} has the same meaning as R^9 , but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

wherein G is

$$\begin{array}{c} \text{---C---(CH}_2\text{)}_r\text{---NR}^{13}\text{R}^{15} \\ || \\ \text{O} \end{array}$$

wherein $r = 0$,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₈-cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

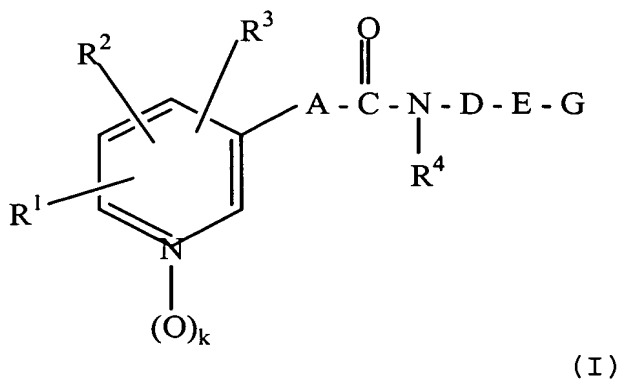
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

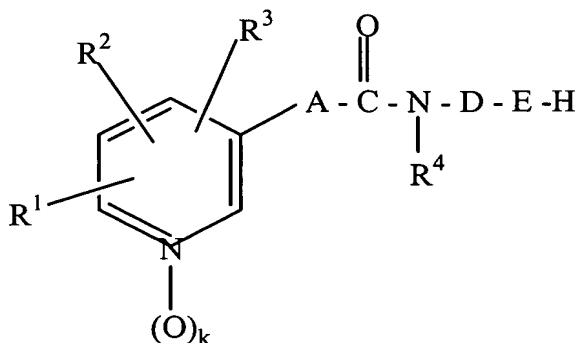
anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group.

39. (Once amended) A method for production of compounds according to formula (I)



(I)

wherein compounds of a formula



are reacted with a compound of formula (VII)



wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_2 - C_6 -alkinyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, C_3 - C_6 -alkinyloxy, benzyloxy, C_1 - C_7 -alkanoyloxy, C_2 - C_7 -alkoxycarbonyloxy, C_1 - C_6 -alkylthio, C_3 - C_6 -alkenylthio, C_3 - C_6 -alkinylthio, C_3 - C_8 -cycloalkyloxy, C_3 - C_8 -cycloalkylthio, C_2 - C_7 -alkoxycarbonyl, aminocarbonyl, C_2 - C_7 -alkylaminocarbonyl, C_3 - C_{13} -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, C_1 - C_6 -alkoxy, benzyloxy and C_1 - C_7 -alkanoyloxy;

R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

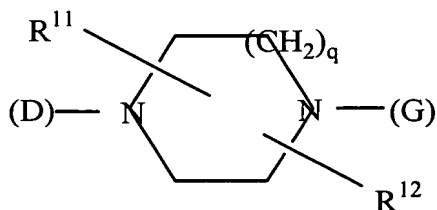
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is

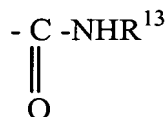


wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom, wherein G is



R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

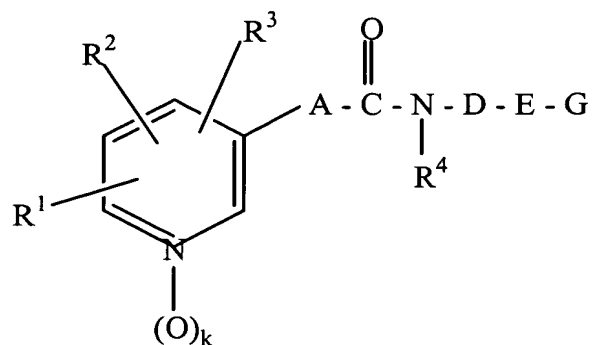
monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group.

49. (Once amended) A method of inhibiting colon, lung, liver and leukemia tumor cell growth in a human or animal body comprising administering to the human or animal body in need thereof an amount of a pharmaceutical composition effective for inhibiting colon, lung, liver and leukemia tumor cell growth, wherein the pharmaceutical composition includes a compound of general formula (I)



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_2 - C_6 -alkinyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, C_3 - C_6 -alkinyloxy, benzyloxy, C_1 - C_7 -alkanoyloxy, C_2 - C_7 -alkoxycarbonyloxy, C_1 - C_6 -alkylthio, C_3 - C_6 -alkenylthio, C_3 - C_6 -alkinylthio, C_3 - C_8 -cycloalkyloxy, C_3 - C_8 -cycloalkylthio, C_2 - C_7 -alkoxycarbonyl, aminocarbonyl, C_2 - C_7 -alkylaminocarbonyl, C_3 - C_{13} -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, C_1 - C_6 -alkoxy, benzyloxy and C_1 - C_7 -alkanoyloxy;

R^3 is selected from the group consisting of hydrogen, halogen, C_1 - C_6 -alkyl, trifluoromethyl and C_1 - C_6 -hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethynylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

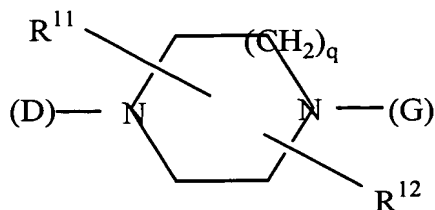
a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkynylene,

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G^1 is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0 to 3,

s is 0 or 1,

R^{13} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -alkinyl, C_3 - C_8 -cycloalkyl,

[saturated or unsaturated four to eight-membered heterocycles,]

saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R^{14} has the same meaning as R^{13} , but is selected independently thereof;

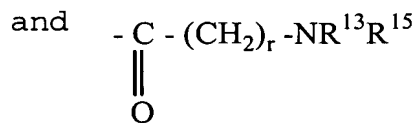
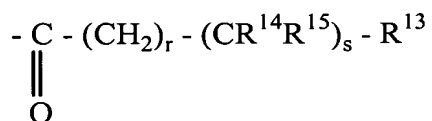
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the hetero-atoms are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrated ring and either directly or over a methylene group,

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

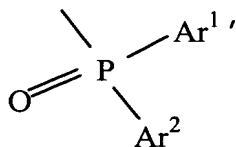
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetro-atoms that are selected from N, S and O;

G^3 is $-\text{SO}_2-(\text{CH}_2)_r-\text{R}^{13}$ (G^3)

wherein r and R^{13} have the above meanings,

G^4 is



wherein

Ar^1 and Ar^2 are selected independently from each other from phenyl, pyridyl or naphthyl,

G^5 is $-\text{COR}^{16}$

R^{16} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, and benzyloxy.